Liquid biopsy predicts immunotherapy response and toxicity in patients with advanced lung cancer

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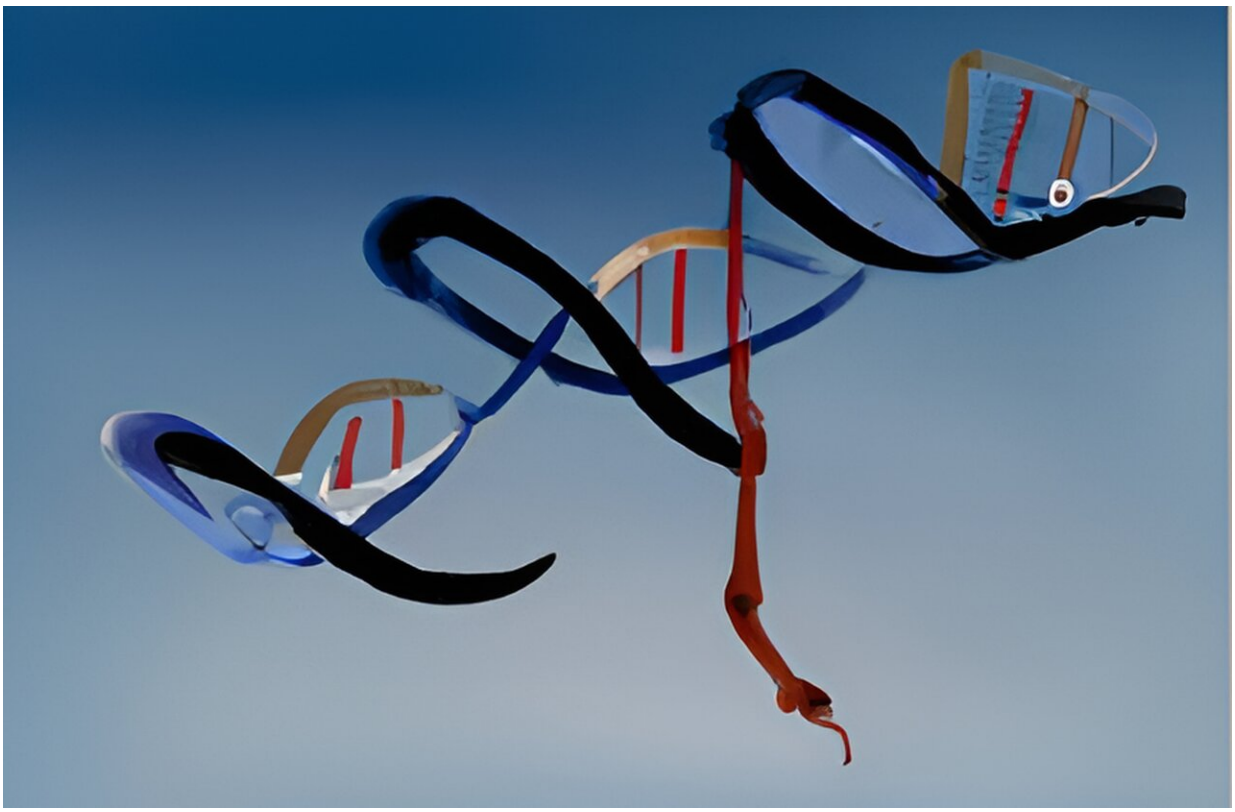

Liquid biopsy to study genetic material shed into bloodstream helps predict response to immunotherapy. Credit: Valsamo "Elsa" Anagnostou using DALL-E

Using a "liquid biopsy" to study genetic material from tumors shed into

the bloodstream together with immune cells could help clinicians predict which patients with advanced lung cancers are responding to immunotherapies and which patients may develop immune-related side effects several months later, according to research directed by investigators at the Johns Hopkins Kimmel Cancer Center, the Bloomberg~Kimmel Institute for Cancer Immunotherapy and Allegheny Health Network Cancer Institute in Pittsburgh.

By monitoring changes in circulating tumor DNA (ctDNA) among 30 patients treated with immunotherapies for metastatic non-small cell lung cancers, the researchers were able to determine molecular response—the clearance of tumor genetic material in the bloodstream—which was significantly associated with progression-free and overall survival.

Serial blood testing was also able to detect an expansion of T cells—immune cells that typically recognize and target foreign or non-self molecules on tumor cells—in patients with immune-related adverse events such as lung tissue inflammation as early as five months ahead of the emergence of clinical symptoms. Similar results were seen in an independent cohort of 49 patients with advanced lung cancers enrolled at the Allegheny Health Network Cancer Institute.

These results were published in the journal *Clinical Cancer Research*.

"Immunotherapy has revolutionized how we take care of patients with lung cancer, but it's been challenging to determine how to assess response," says lead study author Joseph Murray, M.D., Ph.D., an assistant professor of oncology and co-director of the Lung Cancer Precision Medicine Center of Excellence at Johns Hopkins.

"We don't have reliable biomarkers, so we rely a lot on imaging and patient symptoms to see how patients are clinically responding. Now, we can use noninvasive tests like this to study response and predict side

effects very early on, and change therapy regimens if necessary.

The test also was able to help understand the clinical outcomes of patients with stable disease on imaging, says senior study author Valsamo "Elsa" Anagnostou, M.D., Ph.D., associate professor of oncology, director of the thoracic oncology biorepository at Johns Hopkins, leader of Precision Oncology Analytics, co-leader of the Johns Hopkins Molecular Tumor Board and co-director of the Lung Cancer Precision Medicine Center of Excellence at Johns Hopkins.

"All of the patients who appeared to have stable disease on imaging tests had very different DNA molecular response patterns that helped predict their overall clinical outcomes," Anagnostou says. "This is a particular subset of patients for whom we may want to with the ongoing efforts of the thoracic oncology group at Johns Hopkins to implement liquid biopsies in clinical decision-making and use liquid biopsies to guide therapeutic decision-making, as ctDNA can rapidly and accurately capture the amount of cancer present."

This work ties in with the ongoing efforts of the thoracic oncology group at Johns Hopkins to implement liquid biopsies in clinical decision-making, through a ctDNA-adaptive clinical trial of chemo-immunotherapy for patients with metastatic lung cancer.

More information: Joseph C. Murray et al, Elucidating the heterogeneity of immunotherapy response and immune-related toxicities by longitudinal ctDNA and immune cell compartment tracking in lung cancer, *Clinical Cancer Research* (2023). DOI: 10.1158/1078-0432.CCR-23-1469

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